

is in DialUnits

? b 410

```
04sep10 11:52:24 User208760 Session D3209.1
$0.53      0.139 DialUnits File1
$0.53 Estimated cost File1
$0.02 TELNET
$0.55 Estimated cost this search
$0.55 Estimated total session cost    0.139 DialUnits
```

File 410:The Chronolog 1991-2010/ Jun
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Set	Items	Description
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? set hi ;set hi

HIGHLIGHT set on as ''

HIGHLIGHT set on as ''

? begin 5,73,155,399

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04sep10 11:52:55 User208760 Session D3209.2
$0.00      0.117 DialUnits File410
$0.00 Estimated cost File410
$0.14 TELNET
$0.14 Estimated cost this search
$0.69 Estimated total session cost    0.257 DialUnits
```

SYSTEM:OS - DIALOG OneSearch

File 5:Biosis Previews(R) 1926-2010/Aug W5

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File 73:EMBASE 1974-2010/Sep 03

(c) 2010 Elsevier B.V.

File 155:MEDLINE(R) 1950-2010/Sep 02

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File 399:CA SEARCH(R) 1967-2010/UD=15310

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IPCR/8 classification codes now searchable as IC=. See HELP NEWSIPCR.

Set	Items	Description
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? e au= mackay charles ?

Ref	Items	Index-term
E1	3	AU=MACKAY CATRIONA
E2	9	AU=MACKAY CHARLES
E3	0	*AU=MACKAY CHARLES ?
E4	161	AU=MACKAY CHARLES R
E5	2	AU=MACKAY CHARLES S
E6	1	AU=MACKAY CHARLES V
E7	1	AU=MACKAY CHRIS
E8	2	AU=MACKAY CHRIS E
E9	2	AU=MACKAY CHRISTINA
E10	3	AU=MACKAY CHRISTOPHER
E11	2	AU=MACKAY CHRISTOPHER E
E12	4	AU=MACKAY CHRISTOPHER I

Enter P or PAGE for more

? s e4

S1 161 AU='MACKAY CHARLES R'

? s s1 and (c5ar)(20n)(antibod? or immunoglobulin? or hybridoma?)

161 S1
1346 C5AR

2746975 ANTIBOD?
1076826 IMMUNOGLOBULIN?
62242 HYBRIDOMA?
206 C5AR(20N)((ANTIBOD? OR IMMUNOGLOBULIN?) OR HYBRIDOMA?)
S2 8 S1 AND (C5AR)(20N)(ANTIBOD? OR IMMUNOGLOBULIN? OR
HYBRIDOMA?)

? rd s2

S3 4 RD S2 (unique items)

? t s3/3/all

3/3/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

0021622438 BIOSIS NO.: 201000301461
The C5a Receptor (C5aR) C5L2 Is a Modulator of C5aR-mediated Signal
Transduction
AUTHOR: Bamberg Claire E; Mackay Charles R; Lee Hyun; Zahra David;
Jackson Jenny; Lim Yun Si; Whitfeld Peter L; Craig Stewart; Corsini Erin;
Lu Bao; Gerard Craig (Reprint); Gerard Norma P
AUTHOR ADDRESS: 320 Longwood Ave, Boston, MA 02115 USA**USA
AUTHOR E-MAIL ADDRESS: craig.gerard@childrens.harvard.edu;
norma.gerard@childrens.harvard.edu
JOURNAL: Journal of Biological Chemistry 285 (10): p7633-7644 MAR 5 2010
2010
ITEM IDENTIFIER: doi:10.1074/jbc.M109.092106
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

0020324765 BIOSIS NO.: 200800371704
Functional roles for C5a receptors in sepsis
AUTHOR: Rittirsch Daniel; Flierl Michael A; Nadeau Brian A; Day Danielle E;
Huber-Lang Markus; Mackay Charles R; Zetoune Firas S; Gerard Norma
P; Cianflone Katherine; Koehl Joerg; Gerard Craig; Sarma J Vidya; Award
Peter (Reprint)
AUTHOR ADDRESS: Univ Michigan, Sch Med, Dept Pathol, 1301 Catherine Rd, Ann
Arbor, MI 48109 USA**USA
AUTHOR E-MAIL ADDRESS: ward@umich.edu
JOURNAL: Nature Medicine 14 (5): p551-557 MAY 2008 2008
ITEM IDENTIFIER: doi:10.1038/nm1753
ISSN: 1078-8956
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

0020247967 BIOSIS NO.: 200800294906
Receptors for complement C5a. The importance of C5aR and the enigmatic role
of C5L2
AUTHOR: Lee Hyun; Whitfeld Peter L; Mackay Charles R (Reprint)

AUTHOR ADDRESS: St Vincents Hosp, Garvan Inst Med Res, Immunol and
Inflammat Dept, 384 Victoria St, Darlinghurst, NSW 2010, Australia**
Australia
AUTHOR E-MAIL ADDRESS: c.mackay@garvan.org.au
JOURNAL: Immunology and Cell Biology 86 (2): p153-160 FEB 2008 2008
ITEM IDENTIFIER: doi:10.1038/sj.icb.7100166
ISSN: 0818-9641
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

3/3/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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19372097 BIOSIS NO.: 200700031838
Human C5aR knock-in mice facilitate the production and assessment of
anti-inflammatory monoclonal antibodies
AUTHOR: Lee Hyun; Zahra David; Vogelzang Alexis; Newton Rebecca; Thatcher
Jenny; Quan Annie; So Trina; Zwirner Joerg; Koentgen Frank; Padkjaer
Soren B; Mackay Fabienne; Whitfeld Peter L; Mackay Charles R
(Reprint)
AUTHOR ADDRESS: Gavan Inst Med Res, Immunol and Inflammat Dept, 384
Victoria St, Darlinghurst, NSW 2010, Australia**Australia
AUTHOR E-MAIL ADDRESS: c.mackay@garvan.org.au
JOURNAL: Nature Biotechnology 24 (10): p1279-1284 OCT 2006 2006
ISSN: 1087-0156
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
? s (c5ar)(20n)(antibod? or immunoglobulin? or hybridoma?)(20n)(second or
extracellular)(20n)(domain or loop?)
1346 C5AR
2746975 ANTIBOD?
1076826 IMMUNOGLOBULIN?
62242 HYBRIDOMA?
1756743 SECOND
777113 EXTRACELLULAR
911482 DOMAIN
365230 LOOP?
S4 9 (C5AR)(20N)(ANTIBOD? OR IMMUNOGLOBULIN? OR
HYBRIDOMA?)(20N)(SECOND OR EXTRACELLULAR)(20N)(DOMAIN OR
LOOP?)
? rd s4
S5 5 RD S4 (unique items)
? t s5/3/all

5/3/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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Jenny; Quan Annie; So Trina; Zwirner Joerg; Koentgen Frank; Padkjaer
Soren B; Mackay Fabienne; Whitfeld Peter L; Mackay Charles R (Reprint)
AUTHOR ADDRESS: Gavan Inst Med Res, Immunol and Inflammat Dept, 384
Victoria St, Darlinghurst, NSW 2010, Australia**Australia
AUTHOR E-MAIL ADDRESS: c.mackay@garvan.org.au

JOURNAL: Nature Biotechnology 24 (10): p1279-1284 OCT 2006 2006
ISSN: 1087-0156
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

5/3/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

15004663 BIOSIS NO.: 199900264323
Evaluation of C3a receptor expression on human leucocytes by the use of
novel monoclonal antibodies
AUTHOR: Zwirner J (Reprint); Goetze O; Begemann G; Kapp A; Kirchhoff K;
Werfel T
AUTHOR ADDRESS: Abteilung Immunologie, Universitaet Goettingen,
Kreuzberggring 57, D-37075, Goettingen, Germany**Germany
JOURNAL: Immunology 97 (1): p166-172 May, 1999 1999
MEDIUM: print
ISSN: 0019-2805
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

5/3/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

11967344 BIOSIS NO.: 199396131760
Probing the human receptor for C5a anaphylatoxin with site-directed
antibodies: Identification of a potential ligand binding site on the
amino terminal domain
AUTHOR: Oppermann Martin; Raedt Ursula; Hebell Thomas; Schmidt Bernhard;
Zimmermann Bodo; Goetze Otto (Reprint)
AUTHOR ADDRESS: Abteilung Immunologie, Kreuzberggring 57, D-37075
Goettingen, Germany**Germany
JOURNAL: Journal of Immunology 151 (7): p3785-3794 1993
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

5/3/4 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2010 Elsevier B.V. All rts. reserv.

0075503149 EMBASE/Medline No: 1993282705
Probing the human receptor for C5a anaphylatoxin with site-directed
antibodies: Identification of a potential ligand binding site on the NH SUB
2- terminal domain
Oppermann M.; Raedt U.; Hebell T.; Schmidt B.; Zimmermann B.; Gotze O.
Department of Immunology, Max Planck Exptl. Medicine Institute, Gottingen
, Germany
CORRESP. AUTHOR/AFFIL: Oppermann M.: Department of Immunology, Max Planck
Exptl. Medicine Institute, Gottingen, Germany

Journal of Immunology (J. IMMUNOL.) (United States) October 8, 1993,
151/7 (3785-3794)

CODEN: JOIMA ISSN: 0022-1767
DOCUMENT TYPE: Journal; Article RECORD TYPE: Abstract
LANGUAGE: English SUMMARY LANGUAGE: English

5/3/5 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2010 Dialog. All rts. reserv.

10843291 PMID: 8376805
Probing the human receptor for C5a anaphylatoxin with site-directed antibodies. Identification of a potential ligand binding site on the NH2-terminal domain.
Oppermann M; Raedt U; Hebell T; Schmidt B; Zimmermann B; Gotze O
Department of Immunology, University of Gottingen, FRG.
Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Oct 1 1993, 151 (7) p3785-94, ISSN 0022-1767--Print 0022-1767--Linking
Journal Code: 2985117R
Publishing Model Print
Document type: Journal Article; Research Support, Non-U.S. Gov't
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
? t s5/7/all

5/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

19372097 BIOSIS NO.: 200700031838
Human C5aR knock-in mice facilitate the production and assessment of anti-inflammatory monoclonal antibodies
AUTHOR: Lee Hyun; Zahra David; Vogelzang Alexis; Newton Rebecca; Thatcher Jenny; Quan Annie; So Trina; Zwirner Joerg; Koentgen Frank; Padkjaer Soren B; Mackay Fabienne; Whitfeld Peter L; Mackay Charles R (Reprint)
AUTHOR ADDRESS: Gavan Inst Med Res, Immunol and Inflamm Dept, 384 Victoria St, Darlinghurst, NSW 2010, Australia**Australia
AUTHOR E-MAIL ADDRESS: c.mackay@garvan.org.au
JOURNAL: Nature Biotechnology 24 (10): p1279-1284 OCT 2006 2006
ISSN: 1087-0156
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Complement component C5a binds C5a receptor (C5aR) and facilitates leukocyte chemotaxis and release of inflammatory mediators. We used neutrophils from human C5aR knock-in mice, in which the mouse C5aR coding region was replaced with that of human C5aR, to immunize wild-type mice and to generate high-affinity antagonist monoclonal ***antibodies*** (mAbs) to human ***C5aR***. These mAbs blocked neutrophil migration to C5a in vitro and, at low doses, both prevented and reversed inflammatory arthritis in the murine K/BxN model. Of similar to 40 mAbs generated to C5aR, all potent inhibitors recognized a small region of the second extracellular ***loop*** that seems to be critical for regulation of receptor activity. Human C5aR knock-in mice not only facilitated production of high-affinity mAbs against an important human therapeutic target but were also useful in preclinical validation of the potency of these antagonists. This strategy should be applicable to other important mAb therapeutics.

5/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

15004663 BIOSIS NO.: 199900264323
Evaluation of C3a receptor expression on human leucocytes by the use of
novel monoclonal antibodies
AUTHOR: Zwirner J (Reprint); Goetze O; Begemann G; Kapp A; Kirchhoff K;
Werfel T
AUTHOR ADDRESS: Abteilung Immunologie, Universitaet Goettingen,
Kreuzberggring 57, D-37075, Goettingen, Germany**Germany
JOURNAL: Immunology 97 (1): p166-172 May, 1999 1999
MEDIUM: print
ISSN: 0019-2805
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Varying results have been published in the past regarding the reactivity of different leucocyte subpopulations, including neutrophils, monocytes and B lymphocytes, to the anaphylatoxin C3a and its degradation product C3a(desArg). To better characterize the cellular distribution of C3a receptor (C3aR) expression, monoclonal antibodies against two different epitopes on the third extracellular domain of the human C3aR were generated. Quantification of C3aR as compared with C5aR densities was performed on peripheral blood leucocytes by quantitative indirect immunofluorescence. Eosinophils and basophils expressed similar numbers of C3aR and ***C5aR*** molecules/cell. On eosinophils $10\,700 \pm 4500$ (mean \pm SD) C3aR and $14\,700 \pm 4100$ C5aR were found, whereas basophils carried 8100 ± 2100 C3aR and $13\,500 \pm 3800$ ***C5aR***. Monocytes expressed approximately six times more C5aR than C3aR molecules on their surface (6000 ± 2500 C3aR versus $34\,100 \pm 9300$ C5aR molecules) whereas on neutrophils, the expression of C5aR was more than 20 times higher than the expression of C3aR (3100 ± 1000 C3aR versus $63\,500 \pm 12\,200$ C5aR). No C3aR expression was detectable on peripheral blood-derived B lymphocytes and on tonsillar B cells before and after stimulation with interleukin-2/Staphylococcus aureus Cowan strain I. Our findings correspond well with the paucity of data on C3a-induced functional activities in monocytes and neutrophils and suggest that eosinophilic and basophilic granulocytes represent the primary effector cells in the peripheral blood which can be stimulated by C3a.

5/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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11967344 BIOSIS NO.: 199396131760
Probing the human receptor for C5a anaphylatoxin with site-directed antibodies: Identification of a potential ligand binding site on the amino terminal domain
AUTHOR: Oppermann Martin; Raedt Ursula; Hebell Thomas; Schmidt Bernhard; Zimmermann Bodo; Goetze Otto (Reprint)
AUTHOR ADDRESS: Abteilung Immunologie, Kreuzberggring 57, D-37075 Goettingen, Germany**Germany
JOURNAL: Journal of Immunology 151 (7): p3785-3794 1993
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Molecular cloning has revealed the DNA sequence of the human receptor for the C5a anaphylatoxin (C5aR). In this study, mAb and polyclonal antibodies with specificities for deduced hydrophilic sequences of the receptor protein were employed to determine the expression and the topography of C5aR on PBL. Evidence was obtained that an antigenically homogenous receptor exists on human neutrophils, eosinophils, and monocytes that binds C5a and C5a(desArg). The assignment of epitopes to extra- or intracellular receptor domains as determined by FACS analysis of intact or permeabilized cells confirmed the general topography of the C5aR that had been predicted by hydropathy analysis. Competitive binding studies were performed to examine whether ***extracellular*** receptor domains participate in ligand binding. The occupation of the receptor by C5a inhibited only the binding of antibodies that were specific for the receptor's aminoterminal ***domain*** (***C5aR*** -EX1). The anti-EX1 mAb S5/1 effectively antagonized C5a/C5a(desArg) biological activity. A heptameric peptide (D-15DKDTLD-21) was identified as the smallest receptor fragment that was recognized by the mAb S5/1 or by polyclonal rabbit anti-EX1 Ig. These results imply that an amino acid sequence rich in aspartate within the receptor aminoterminal represents both an immunodominant epitope and a ligand binding site on the C5aR.

5/7/4 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
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0075503149 EMBASE/Medline No: 1993282705
Probing the human receptor for C5a anaphylatoxin with site-directed antibodies: Identification of a potential ligand binding site on the NH SUB 2- terminal domain
Oppermann M.; Raedt U.; Hebell T.; Schmidt B.; Zimmermann B.; Gotze O.
Department of Immunology, Max Planck Exptl. Medicine Institute, Gottingen, Germany
CORRESP. AUTHOR/AFFIL: Oppermann M.: Department of Immunology, Max Planck Exptl. Medicine Institute, Gottingen, Germany

Journal of Immunology (J. IMMUNOL.) (United States) October 8, 1993, 151/7 (3785-3794)
CODEN: JOIMA ISSN: 0022-1767
DOCUMENT TYPE: Journal; Article RECORD TYPE: Abstract
LANGUAGE: English SUMMARY LANGUAGE: English

Molecular cloning has revealed the DNA sequence of the human receptor for the C5a anaphylatoxin (C5aR). In this study, mAb and polyclonal antibodies with specificities for deduced hydrophilic sequences of the receptor protein were employed to determine the expression and the topography of C5aR on PBL. Evidence was obtained that an antigenically homogenous receptor exists on human neutrophils, eosinophils, and monocytes that binds C5a and C5a(desArg). The assignment of epitopes to extra- or intracellular receptor domains as determined by FACS analysis of intact or permeabilized cells confirmed the general topography of the C5aR that had been predicted by hydropathy analysis. Competitive binding studies were performed to examine whether extracellular receptor domains participate in ligand binding. The occupation of the receptor by C5a inhibited only the binding of antibodies that were specific for the receptor's aminoterminal ***domain*** (***C5aR*** -EX1). The anti-EX1 mAb S5/1 effectively antagonized C5a/C5a(desArg) biological activity. A heptameric peptide (D SUB 15DKDTLD SUB 21) was identified as the smallest

receptor fragment that was recognized by the mAb S5/1 or by polyclonal rabbit anti- EX1 Ig. These results imply that an amino acid sequence rich in aspartate within the receptor aminotermminus represents both an immunodominant epitope and a ligand binding site on the C5aR.

5/7/5 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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10843291 PMID: 8376805

Probing the human receptor for C5a anaphylatoxin with site-directed antibodies. Identification of a potential ligand binding site on the NH2-terminal domain.

Oppermann M; Raedt U; Hebell T; Schmidt B; Zimmermann B; Gotze O

Department of Immunology, University of Gottingen, FRG.

Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Oct 1 1993, 151 (7) p3785-94, ISSN 0022-1767--Print 0022-1767--Linking

Journal Code: 2985117R

Publishing Model Print

Document type: Journal Article; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Molecular cloning has revealed the DNA sequence of the human receptor for the C5a anaphylatoxin (C5aR). In this study, mAb and polyclonal antibodies with specificities for deduced hydrophilic sequences of the receptor protein were employed to determine the expression and the topography of C5aR on PBL. Evidence was obtained that an antigenically homogenous receptor exists on human neutrophils, eosinophils, and monocytes that binds C5a and C5a(desArg). The assignment of epitopes to extra- or intracellular receptor domains as determined by FACS analysis of intact or permeabilized cells confirmed the general topography of the C5aR that had been predicted by hydropathy analysis. Competitive binding studies were performed to examine whether extracellular receptor domains participate in ligand binding. The occupation of the receptor by C5a inhibited only the binding of antibodies that were specific for the receptor's aminoterminal ***domain*** (***C5aR*** -EX1). The anti-EX1 mAb S5/1 effectively antagonized C5a/C5a(desArg) biological activity. A heptameric peptide (D15DKDTLD21) was identified as the smallest receptor fragment that was recognized by the mAb S5/1 or by polyclonal rabbit anti-EX1 lg. These results imply that an amino acid sequence rich in aspartate within the receptor aminotermminus represents both an immunodominant epitope and a ligand binding site on the C5aR.

Record Date Created: 19931021

Record Date Completed: 19931021

? ds

Set	Items	Description
S1	161	AU='MACKAY CHARLES R'
S2	8	S1 AND (C5AR) (20N) (ANTIBOD? OR IMMUNOGLOBULIN? OR HYBRIDOM-A?)
S3	4	RD S2 (unique items)
S4	9	(C5AR) (20N) (ANTIBOD? OR IMMUNOGLOBULIN? OR HYBRIDOMA?) (20N-) (SECOND OR EXTRACELLULAR) (20N) (DOMAIN OR LOOP?)
S5	5	RD S4 (unique items)
? s		(c5ar) and (antibod? or immunoglobulin? or hybridoma?) (20n) (second or extracellular) (20n) (domain or loop?)
	1346	C5AR
	2746975	ANTIBOD?
	1076826	IMMUNOGLOBULIN?

62242 HYBRIDOMA?
 1756743 SECOND
 777113 EXTRACELLULAR
 911482 DOMAIN
 365230 LOOP?
 10432 ((ANTIBOD? OR IMMUNOGLOBULIN?) OR HYBRIDOMA?) (20N) (SECOND
 OR EXTRACELLULAR) (20N) (DOMAIN OR LOOP?)
 S6 6 (C5AR) AND (ANTIBOD? OR IMMUNOGLOBULIN? OR
 HYBRIDOMA?) (20N) (SECOND OR EXTRACELLULAR) (20N) (DOMAIN OR
 LOOP?)

? rd s6

S7 4 RD S6 (unique items)

? t s7/3/all

7/3/1 (Item 1 from file: 5)
 DIALOG(R)File 5:Biosis Previews(R)
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15004663 BIOSIS NO.: 199900264323
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 AUTHOR: Zwirner J (Reprint); Goetze O; Begemann G; Kapp A; Kirchhoff K;
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 AUTHOR ADDRESS: Abteilung Immunologie, Universitaet Goettingen,
 Kreuzberggring 57, D-37075, Goettingen, Germany**Germany
 JOURNAL: Immunology 97 (1): p166-172 May, 1999 1999
 MEDIUM: print
 ISSN: 0019-2805
 DOCUMENT TYPE: Article
 RECORD TYPE: Abstract
 LANGUAGE: English

7/3/2 (Item 2 from file: 5)
 DIALOG(R)File 5:Biosis Previews(R)
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11967344 BIOSIS NO.: 199396131760
 Probing the human receptor for C5a anaphylatoxin with site-directed
 antibodies: Identification of a potential ligand binding site on the
 amino terminal domain
 AUTHOR: Oppermann Martin; Raedt Ursula; Hebell Thomas; Schmidt Bernhard;
 Zimmermann Bodo; Goetze Otto (Reprint)
 AUTHOR ADDRESS: Abteilung Immunologie, Kreuzberggring 57, D-37075
 Goettingen, Germany**Germany
 JOURNAL: Journal of Immunology 151 (7): p3785-3794 1993
 ISSN: 0022-1767
 DOCUMENT TYPE: Article
 RECORD TYPE: Abstract
 LANGUAGE: English

7/3/3 (Item 1 from file: 73)
 DIALOG(R)File 73:EMBASE
 (c) 2010 Elsevier B.V. All rts. reserv.

0075503149 EMBASE/Medline No: 1993282705
 Probing the human receptor for C5a anaphylatoxin with site-directed
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 Oppermann M.; Raedt U.; Hebell T.; Schmidt B.; Zimmermann B.; Gotze O.

Department of Immunology, Max Planck Exptl. Medicine Institute, Gottingen
, Germany
CORRESP. AUTHOR/AFFIL: Oppermann M.: Department of Immunology, Max Planck
Exptl. Medicine Institute, Gottingen, Germany

Journal of Immunology (J. IMMUNOL.) (United States) October 8, 1993,
151/7 (3785-3794)
CODEN: JOIMA ISSN: 0022-1767
DOCUMENT TYPE: Journal; Article RECORD TYPE: Abstract
LANGUAGE: English SUMMARY LANGUAGE: English

7/3/4 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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10843291 PMID: 8376805
Probing the human receptor for C5a anaphylatoxin with site-directed
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Oppermann M; Raedt U; Hebell T; Schmidt B; Zimmermann B; Gotze O
Department of Immunology, University of Gottingen, FRG.
Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Oct 1
1993, 151 (7) p3785-94, ISSN 0022-1767--Print 0022-1767--Linking
Journal Code: 2985117R
Publishing Model Print
Document type: Journal Article; Research Support, Non-U.S. Gov't
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
? s (c5ar)(20n)(second or extracellular)(20n)(domain or loop?)
1346 C5AR
1756743 SECOND
777113 EXTRACELLULAR
911482 DOMAIN
365230 LOOP?
S8 47 (C5AR)(20N)(SECOND OR EXTRACELLULAR)(20N)(DOMAIN OR
LOOP?)
? rd s8
S9 18 RD S8 (unique items)
? t s9/3/all

9/3/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0020252046 BIOSIS NO.: 200800298985
Modeling molecular mechanisms of binding of the anaphylatoxin C5a to the
C5a receptor
AUTHOR: Nikiforovich Gregory V (Reprint); Marshall Garland R; Baranski
Thomas J
AUTHOR ADDRESS: Washington Univ, Sch Med, Ctr Computat Biol, Dept Biochem
and Mol Biophys, St Louis, MO 63110 USA**USA
AUTHOR E-MAIL ADDRESS: gregory@ccb.wustl.edu
JOURNAL: Biochemistry 47 (10): p3117-3130 MAR 11 2008 2008
ITEM IDENTIFIER: doi:10.1021/bi702321a
ISSN: 0006-2960
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

9/3/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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AUTHOR: Lee Hyun; Zahra David; Vogelzang Alexis; Newton Rebecca; Thatcher
Jenny; Quan Annie; So Trina; Zwirner Joerg; Koentgen Frank; Padkjaer
Soren B; Mackay Fabienne; Whitfeld Peter L; Mackay Charles R (Reprint)
AUTHOR ADDRESS: Gavan Inst Med Res, Immunol and Inflammat Dept, 384
Victoria St, Darlinghurst, NSW 2010, Australia**Australia
AUTHOR E-MAIL ADDRESS: c.mackay@garvan.org.au
JOURNAL: Nature Biotechnology 24 (10): p1279-1284 OCT 2006 2006
ISSN: 1087-0156
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

9/3/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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18692804 BIOSIS NO.: 200600038199
Characterization of a C3a receptor in rainbow trout and Xenopus: The first
identification of C3a receptors in nonmammalian species
AUTHOR: Boshra Hani; Wang Tiehui; Hove-Madsen Leif; Hansen John; Li Jun;
Matlapudi Anjun; Secombes Christopher J; Tort Lluís; Sunyer J Oriol
(Reprint)
AUTHOR ADDRESS: Univ Penn, Sch Vet Med, Dept Pathobiol, 3800 Spruce St, 413
Rosenthal, Philadelphia, PA 19104 USA**USA
AUTHOR E-MAIL ADDRESS: sunyer@vet.upenn.edu
JOURNAL: Journal of Immunology 175 (4): p2427-2437 AUG 15 2005 2005
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

9/3/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

18321695 BIOSIS NO.: 200510016195
Essential role for the second extracellular loop in C5a receptor activation
AUTHOR: Klco Jeffery M; Wiegand Christina B; Narzinski Kirk; Baranski
Thomas J (Reprint)
AUTHOR ADDRESS: Washington Univ, Sch Med, Dept Med, Campus Box 8127, 660 S
Euclid Ave, St Louis, MO 63110 USA**USA
AUTHOR E-MAIL ADDRESS: baranski@wustl.edu
JOURNAL: Nature Structural & Molecular Biology 12 (4): p320-326 APR 05
2005
ISSN: 1545-9985
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

9/3/5 (Item 5 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)
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18242742 BIOSIS NO.: 200500149807

Residues 10-18 within the C5a receptor N terminus compose a binding domain
for chemotaxis inhibitory protein of Staphylococcus aureus

AUTHOR: Postma Bent; Kleibeuker Wendy; Poppelier Miriam J J G; Boonstra
Miranda; van Kessel Kok P M; van Strijp Jos A G; de Haas Carla J C
(Reprint)

AUTHOR ADDRESS: Eijkman Winkler Inst, Univ Med Ctr Utrecht,
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JOURNAL: Journal of Biological Chemistry 280 (3): p2020-2027 January 21,
2005 2005

MEDIUM: print

ISSN: 0021-9258

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

9/3/6 (Item 6 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

17759413 BIOSIS NO.: 200400130170

Molecular cloning and characterization of rainbow trout (Oncorhynchus
mykiss) C5a anaphylatoxin receptor.

AUTHOR: Fujiki Kazuhiro; Liu Lei; Sundick Roy S; Dixon Brian (Reprint)

AUTHOR ADDRESS: Department of Biology, University of Waterloo, 200

University Avenue West, Waterloo, ON, N2L 3G1, Canada**Canada

AUTHOR E-MAIL ADDRESS: bdixon@sciborg.uwaterloo.ca

JOURNAL: Immunogenetics 55 (9): p640-646 December 2003 2003

MEDIUM: print

ISSN: 0093-7711

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

9/3/7 (Item 7 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

16142348 BIOSIS NO.: 200100314187

Modulation of ligand selectivity by mutation of the first extracellular
loop of the human C5a receptor

AUTHOR: Cain Stuart A; Woodruff Trent M; Taylor Stephen M; Fairlie David P;
Sanderson Sam D; Monk Peter N (Reprint)

AUTHOR ADDRESS: Section of Neurology, Division of Clinical Sciences,
University of Sheffield Medical School, Beech Hill Road, Sheffield, S10
2RX, UK**UK

JOURNAL: Biochemical Pharmacology 61 (12): p1571-1579 15 June, 2001 2001

MEDIUM: print

ISSN: 0006-2952

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

9/3/8 (Item 8 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

15319438 BIOSIS NO.: 200000037751
Identification of ligand effector binding sites in transmembrane regions of
the human G protein-coupled C3a receptor
AUTHOR: Sun Jianzhong; Ember Julia A; Chao Ta-Hsiang; Fukuoka Yoshihiro; Ye
Richard D; Hugli Tony E (Reprint)
AUTHOR ADDRESS: Department of Immunology/IMM-18, The Scripps Research
Institute, La Jolla, CA, 92037, USA**USA
JOURNAL: Protein Science 8 (11): p2304-2311 Nov., 1999 1999
MEDIUM: print
ISSN: 0961-8368
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

9/3/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

15004663 BIOSIS NO.: 199900264323
Evaluation of C3a receptor expression on human leucocytes by the use of
novel monoclonal antibodies
AUTHOR: Zwirner J (Reprint); Goetze O; Begemann G; Kapp A; Kirchhoff K;
Werfel T
AUTHOR ADDRESS: Abteilung Immunologie, Universitaet Goettingen,
Kreuzberggring 57, D-37075, Goettingen, Germany**Germany
JOURNAL: Immunology 97 (1): p166-172 May, 1999 1999
MEDIUM: print
ISSN: 0019-2805
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

9/3/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

14975997 BIOSIS NO.: 199900235657
Chimeric receptors of the human C3a receptor and C5a receptor (CD88)
AUTHOR: Crass Torsten; Ames Robert S; Sarau Henry M; Tornetta Mark A; Foley
James J; Koehl Joerg; Klos Andreas; Bautsch Wilfried (Reprint)
AUTHOR ADDRESS: Inst. of Medical Microbiology, Hannover Medical School,
Carl-Neuberg-Str. 1, D-30623, Hannover, Germany**Germany
JOURNAL: Journal of Biological Chemistry 274 (13): p8367-8370 March 26,
1999 1999
MEDIUM: print
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

9/3/11 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

14418392 BIOSIS NO.: 199800212639

Cloning and characterization of the guinea pig C5a anaphylatoxin receptor:
Interspecies diversity among the C5a receptors
AUTHOR: Fukuoka Yoshihiro; Ember Julia A; Yasui Akira; Hugli Tony E
(Reprint)
AUTHOR ADDRESS: Dep. Immunol., Scripps Res. Inst., 10550 North Torrey Pines
Rd., La Jolla, CA 92037, USA**USA
JOURNAL: International Immunology 10 (3): p275-283 March, 1998 1998
MEDIUM: print
ISSN: 0953-8178
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

9/3/12 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

13625822 BIOSIS NO.: 199699259882
Molecular evolution of the N-formyl peptide and C5a receptors in non-human
primates
AUTHOR: Alvarez Victoria; Coto Eliecer; Setien Fernando; Gonzalez-Roces
Severino; Lopez-Larrea Carlos (Reprint)
AUTHOR ADDRESS: Serv. Inmunol., Hosp. Central de Asturias, 33006 Oviedo,
Spain**Spain
JOURNAL: Immunogenetics 44 (6): p446-452 1996 1996
ISSN: 0093-7711
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

9/3/13 (Item 13 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

12165081 BIOSIS NO.: 199497186366
The NH-2-terminal region of C5aR but not that of FPR is critical for both
protein transport and ligand binding
AUTHOR: Mery Laurence (Reprint); Boulay Francois
AUTHOR ADDRESS: DBMS/Lab. Biochimie, Centre d'Etudes Nucleaires, 85 X,
38041 Grenoble Cedex, France**France
JOURNAL: Journal of Biological Chemistry 269 (5): p3457-3463 1994 1994
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

9/3/14 (Item 14 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

12112529 BIOSIS NO.: 199497133814
Evidence that the extracellular N-terminal domain of C5aR
contains amino-acid residues crucial for C5a binding
AUTHOR: Mery Laurence; Boulay Francois
AUTHOR ADDRESS: DBMS/Laboratoire de Biochimie (CNRS/URA 1130), Centre
d'Etudes Nucleaires, 85X, 38041 Grenoble Cedex, France**France
JOURNAL: European Journal of Haematology 51 (5): p282-287 1993 1993
ISSN: 0902-4441

DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

9/3/15 (Item 15 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2010 The Thomson Corporation. All rts. reserv.

11967344 BIOSIS NO.: 199396131760
Probing the human receptor for C5a anaphylatoxin with site-directed
antibodies: Identification of a potential ligand binding site on the
amino terminal domain
AUTHOR: Oppermann Martin; Raedt Ursula; Hebell Thomas; Schmidt Bernhard;
Zimmermann Bodo; Goetze Otto (Reprint)
AUTHOR ADDRESS: Abteilung Immunologie, Kreuzberggring 57, D-37075
Goettingen, Germany**Germany
JOURNAL: Journal of Immunology 151 (7): p3785-3794 1993
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

9/3/16 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2010 Elsevier B.V. All rts. reserv.

0075503149 EMBASE/Medline No: 1993282705
Probing the human receptor for C5a anaphylatoxin with site-directed
antibodies: Identification of a potential ligand binding site on the NH SUB
2- terminal domain
Oppermann M.; Raedt U.; Hebell T.; Schmidt B.; Zimmermann B.; Gotze O.
Department of Immunology, Max Planck Exptl. Medicine Institute, Gottingen
, Germany
CORRESP. AUTHOR/AFFIL: Oppermann M.: Department of Immunology, Max Planck
Exptl. Medicine Institute, Gottingen, Germany

Journal of Immunology (J. IMMUNOL.) (United States) October 8, 1993,
151/7 (3785-3794)
CODEN: JOIMA ISSN: 0022-1767
DOCUMENT TYPE: Journal; Article RECORD TYPE: Abstract
LANGUAGE: English SUMMARY LANGUAGE: English

9/3/17 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2010 Dialog. All rts. reserv.

10843291 PMID: 8376805
Probing the human receptor for C5a anaphylatoxin with site-directed
antibodies. Identification of a potential ligand binding site on the
NH2-terminal domain.
Oppermann M; Raedt U; Hebell T; Schmidt B; Zimmermann B; Gotze O
Department of Immunology, University of Gottingen, FRG.
Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Oct 1
1993, 151 (7) p3785-94, ISSN 0022-1767--Print 0022-1767--Linking
Journal Code: 2985117R
Publishing Model Print
Document type: Journal Article; Research Support, Non-U.S. Gov't
Languages: ENGLISH

Main Citation Owner: NLM
Record type: MEDLINE; Completed

9/3/18 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 2010 American Chemical Society. All rts. reserv.

143092076 CA: 143(6)92076b PATENT
Transgenic non-human mammal comprising a polynucleotide encoding human or humanized complement C5a receptor (C5aR), and uses in drug screening
INVENTOR(AUTHOR): MacKay, Charles Reay
LOCATION: Australia
ASSIGNEE: G2 Inflammation Pty. Ltd.
PATENT: PCT International ; WO 200560739 A1 DATE: 20050707
APPLICATION: WO 2004AU1844 (20041224) *AU 2003907150 (20031224)
PAGES: 98 pp. CODEN: PIXXD2 LANGUAGE: English
PATENT CLASSIFICATIONS:
CLASS: A01K-067/027A; C12N-015/00B
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BW; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; EG; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NA; NI; NO; NZ; OM; PG; PH; PL; PT; RO; RU; SC; SD; SE; SG; SK; SL; SY; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VC; VN; YU; ZA; ZM; ZW DESIGNATED REGIONAL: BW; GH; GM; KE; LS; MW; MZ; NA; SD; SL; SZ; TZ; UG; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM; AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; HU; IE; IS; IT; LT; LU; MC; NL; PL; PT; RO; SE; SI; SK; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG
? t s9/7/4,7,10,13,14

9/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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18321695 BIOSIS NO.: 200510016195
Essential role for the second extracellular loop in C5a receptor activation
AUTHOR: Klco Jeffery M; Wiegand Christina B; Narzinski Kirk; Baranski Thomas J (Reprint)
AUTHOR ADDRESS: Washington Univ, Sch Med, Dept Med, Campus Box 8127,660 S Euclid Ave, St Louis, MO 63110 USA**USA
AUTHOR E-MAIL ADDRESS: baranski@wustl.edu
JOURNAL: Nature Structural & Molecular Biology 12 (4): p320-326 APR 05 2005
ISSN: 1545-9985
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: More than 90% of G protein - coupled receptors (GPCRs) contain a disulfide bridge that tethers the second extracellular ***loop*** (EC2) to the third transmembrane helix. To determine the importance of EC2 and its disulfide bridge in receptor activation, we subjected this region of the complement factor 5a receptor (C5aR) to random saturation mutagenesis and screened for functional receptors in yeast. The cysteine forming the disulfide bridge was the only conserved residue in the EC2-mutated receptors. Notably, - 80% of the functional receptors exhibited potent constitutive activity. These results demonstrate an unexpected role for EC2 as a negative regulator of C5a receptor activation. We propose that in other GPCRs, EC2 might serve a similar role by stabilizing the inactive state of the receptor.

9/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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16142348 BIOSIS NO.: 200100314187
Modulation of ligand selectivity by mutation of the first extracellular
loop of the human C5a receptor
AUTHOR: Cain Stuart A; Woodruff Trent M; Taylor Stephen M; Fairlie David P;
Sanderson Sam D; Monk Peter N (Reprint)
AUTHOR ADDRESS: Section of Neurology, Division of Clinical Sciences,
University of Sheffield Medical School, Beech Hill Road, Sheffield, S10
2RX, UK**UK
JOURNAL: Biochemical Pharmacology 61 (12): p1571-1579 15 June, 2001 2001
MEDIUM: print
ISSN: 0006-2952
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The cyclic C5a receptor antagonist, phenylalanine
(L-ornithine-proline-D-cyclohexylalanine-tryptophan-arginine)
(F-(OPchaWR)), has approx1000-fold less affinity for the C5a receptor (
C5aR) on murine polymorphonuclear leukocytes than on human.
Analysis of C5aR from different species shows that a possible cause
of this difference is the variation in the sequence of the first
extracellular ***loop*** of the receptor. The mouse receptor
contains Y at a position analogous to P103 in the human receptor, and D
at G105. To test this hypothesis, we expressed human ***C5aR*** mutants
(P103 Y, G105D and the double mutant, P103Y/G105D) in RBL-2H3 cells and
investigated the effects of these mutations on binding affinity and
receptor activation. All three mutant receptors had a higher affinity for
human C5a than the wild-type receptor, but showed no significant
difference in the ability of F-(OPchaWR) to inhibit human C5a binding.
However, all of the mutant receptors had substantially lower affinities
for the weak agonist, C5a des Arg74 (C5adR74), and two altered receptors
(G105D and P103Y/G105D) had much lower affinities for the C-terminal C5a
agonist peptide analogue,
L-tyrosine-serine-phenylalanine-lysine-proline-methionine-proline-leucine
-D-alanine-arginine (YSFKPMPLaR). Although it is unlikely that
differences at these residues are responsible for variations in the
potency of F-(OPchaWR) across species, residues in the first
extracellular loop are clearly involved in the recognition of both C5a
and C5a agonists. The complex effects of mutating these residues on the
affinity and response to C5a, C5adR74, and the peptide analogues provide
evidence of different binding modes for these ligands on the C5aR.

9/7/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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14975997 BIOSIS NO.: 199900235657
Chimeric receptors of the human C3a receptor and C5a receptor (CD88)
AUTHOR: Crass Torsten; Ames Robert S; Sarau Henry M; Tornetta Mark A; Foley
James J; Koehl Joerg; Klos Andreas; Bautsch Wilfried (Reprint)
AUTHOR ADDRESS: Inst. of Medical Microbiology, Hannover Medical School,
Carl-Neuberg-Str. 1, D-30623, Hannover, Germany**Germany
JOURNAL: Journal of Biological Chemistry 274 (13): p8367-8370 March 26,
1999 1999

MEDIUM: print
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Chimeras were generated between the human anaphylatoxin C3a and C5a receptors (C3aR and C5aR, respectively) to define the structural requirements for ligand binding and discrimination. Chimeric receptors were generated by systematically exchanging between the two receptors four receptor modules (the N terminus, transmembrane regions 1 to 4, the second extracellular loop, and transmembrane region 5 to the C terminus). The mutants were transiently expressed in HEK-293 cells (with or without Galpha-16) and analyzed for cell surface expression, binding of C3a and C5a, and functional responsiveness (calcium mobilization) toward C3a, C5a, and a C3a as well as a C5a analogue peptide. The data indicate that in both anaphylatoxin receptors the transmembrane regions and the second extracellular loop act as a functional unit that is disrupted by any reciprocal exchange. N-terminal substitution confirmed the two-binding site model for the human C5aR, in which the receptor N terminus is required for high affinity binding of the native ligand but not a C5a analogue peptide. In contrast, the human C3a receptor did not require the original N terminus for high affinity binding of and activation by C3a, a result that was confirmed by N-terminal deletion mutants. This indicates a completely different binding mode of the anaphylatoxins to their corresponding receptors. The C5a analogue peptide, but not C5a, was an agonist of the C3aR. Replacement of the C3aR N terminus by the C5aR sequence, however, lead to the generation of a true hybrid C3a/C5a receptor, which bound and functionally responded to both ligands, C3a and C5a.

9/7/13 (Item 13 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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12165081 BIOSIS NO.: 199497186366
The NH-2-terminal region of C5aR but not that of FPR is critical for both protein transport and ligand binding
AUTHOR: Mery Laurence (Reprint); Boulay Francois
AUTHOR ADDRESS: DBMS/Lab. Biochimie, Centre d'Etudes Nucleaires, 85 X, 38041 Grenoble Cedex, France**France
JOURNAL: Journal of Biological Chemistry 269 (5): p3457-3463 1994 1994
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The N-formylated tripeptide, formylmethionylleucylphenylalanine (fMLP), and the 74-amino-acid long human C5a anaphylatoxin activate phagocytic cells via two structurally related G protein-coupled receptors (FPR and C5aR), which are 34% identical in amino acid sequence. C5aR chimeras were constructed in which the entire NH-2-terminal extracellular sequence or part of it was replaced by the counterparts from FPR or FPRH. Although the NH-2-terminal region of C5aR presents an extremely high interspecies variability, substitution of the entire NH-2-terminal sequence of C5aR by that of FPR or FPRH surprisingly resulted in chimeras that were apparently retained in the endoplasmic reticulum. In contrast, when the NH-2-terminal domain of FPR was replaced by the corresponding

region from C5aR or FPRH normal expression to the plasma membrane and high affinity binding of N-formylated peptides were observed. Thus, the NH-2-terminal region of C5aR, in contradistinction to that of FPR, seems to be required either for the translocation of C5aR through the ER membrane or for correct folding and sorting of C5aR to the plasma membrane. Replacement of the first 8 residues of C5aR by the corresponding region of FPR did not alter the cellular transport and the C5a binding capacity, whereas the exchange of the first 13 residues resulted in a chimera that was readily transported to the plasma membrane but showed no capability to bind C5a. Mutations of Asp into Asn in the NH-2-terminal segment of C5aR further indicated that negative charges are required to endow the receptor with a C5a binding capacity. The residues critical for binding are either involved directly by interacting with cationic residues of C5a, or indirectly by influencing the overall structure of the ligand-binding site.

9/7/14 (Item 14 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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12112529 BIOSIS NO.: 199497133814
Evidence that the extracellular N-terminal domain of C5aR
contains amino-acid residues crucial for C5a binding
AUTHOR: Mery Laurence; Boulay Francois
AUTHOR ADDRESS: DBMS/Laboratoire de Biochimie (CNRS/URA 1130), Centre
d'Etudes Nucleaires, 85X, 38041 Grenoble Cedex, France**France
JOURNAL: European Journal of Haematology 51 (5): p282-287 1993 1993
ISSN: 0902-4441
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The human C5a anaphylatoxin is a cationic 74 amino-acid long glycopeptide which derives from proteolysis of the fifth component of complement. It interacts with high affinity with a receptor that belongs to the G protein-coupled receptor superfamily. Several studies have previously suggested that multiple contact points between C5a and the receptor are required to achieve high-affinity interaction. However, at the receptor level little is known about the sites of interaction with C5a. We have investigated by in vitro mutagenesis whether the N-terminal extracellular sequence of the C5a receptor, which is rich in aspartic acid residues, could play some role in C5a binding. Conversion of Asp-10 into asparagine did not impair the level of expression at the plasma membrane, nor did it alter the affinity for C5a. However, we consistently observed a discrepancy between an apparent high level of surface expression and a weak capacity to bind C5a with high affinity, suggesting that many receptor molecules, although present on the cell surface, might be misfolded and unable to bind C5a. Replacement of Pro-9 by an isoleucine had little effect, if any, on either the affinity or the C5a-binding capacity, whereas the conversion of Pro-36 into leucine dramatically reduced the expression of high-affinity receptor at the cell surface. N-glycosylation of human C5a receptor was found to be dispensable for the function of the receptor.

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